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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference L2256 PCT S3	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US2004/035804	International filing date *(day/month/year)* 27.10.2004	Priority date *(day/month/year)* 31.10.2003
International Patent Classification (IPC) or national classification and IPC A61K38/21, A61P35/00, A61P31/12, A61P37/00		
Applicant PEPGEN CORPORATION		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
31.08.2005	13.03.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Merckling-Ruiz, V Telephone No. +49 89 2399-8590

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/035804

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-49 as originally filed

Sequence listings part of the description, Pages

1-3 as originally filed

Claims, Numbers

1-7 received on 13.02.2006 with letter of 13.02.2006

Drawings, Sheets

1-17 as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/035804

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-6
	No:	Claims	7
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-7
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

1. Reference is made to the following documents :

D1: WO 03/061728 A (Pepgen Corp., published 31.07.2003)

D2: SOOS J M ET AL: "ORAL FEEDING OF INTERFERON TAU CAN PREVENT THE ACUTE AND CHRONIC RELAPSING FORMS OF EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS" JOURNAL OF NEUROIMMUNOLOGY, ELSEVIER SCIENCE PUBLISHERS BV, XX, vol. 75, no. ½, May 1997 (1997-05), pages 43-50, XP000676399 ISSN: 0165-5728

D3: WO 02/06343 A (PEPGEN CORPORATION) 24 January 2002 (2002-01-24)

D4: WO 96/28183 A (UNIVERSITY OF FLORIDA; SOOS, JEANNE, M; SCHIFFENBAUER, JOEL; JOHNSON,) 19 September 1996 (1996-09-19)

D5: US-A-5 738 845 (IMAKAWA ET AL) 14 April 1998 (1998-04-14)

D6: NAKAJIMA A ET AL: "INDUCTION OF BLOOD 2',5'-OLIGOADENYLATE SYNTHETASE ACTIVITY IN MICE BY GASTRIC ADMINISTRATION OF OVINE IFN-TAU" JOURNAL OF INTERFERON AND CYTOKINE RESEARCH, MARY ANN LIEBERT, NEW YORK, NY, US, vol. 22, no. 3, March 2002 (2002-03), pages 397-402, XP008009443 ISSN: 1079-9907

NB : D1 was previously wrongly referenced as WO 03/061720. The right reference is WO 03/061728 and has now been corrected.

Regarding point V

2. D3 discloses orally administered compositions comprising IFNT at a dosage greater than 10^9 U/day (see example 3 table 2 of D3, which is identical to example 4 and table 2 of the present application). Claim 7, which is directed to a first medical use, is anticipated by D3.

2.1 None of the documents that disclose the use of IFNT for treating autoimmune diseases or cancer (D1, D2, D4 and D4) discloses oral administration of IFNT at a dosage greater than 10^9 U/day. Second medical use claims 1-6 are novel.

3. The problem underlying the application is to provide an alternative treatment for autoimmune diseases and cancer. The problem is allegedly solved by administering orally more than 10^9 U/day of IFNT.

D1, D2 and D4 teach the use orally administered IFNT for treating autoimmune diseases. The dosage used is 10^5 to $5x10^5$ U/day. These documents disclose exactly the same experiments as the ones labelled example 1 and examples 5-11 in the present application.

D5 teaches the use of IFNT for treating cancer. No oral administration is disclosed, IFNT was injected to mice at a dose of 10^5 U/day.

D3 is limited to a therapeutic use for treating hepatitis C infection, but discloses oral administration and the dosage of greater than 10^9 U/day (same as example 4 of application).

Firstly, the subject-matter of claim 1 is obvious over any of D1, D2 or D4 combined with the teaching of D3.

Secondly, the only example of the application wherein a dosage of 10^9 U/day of IFNT is used is example 4, which relates to HCV infection and which is the same as in D3. No effect of such a high dosage of oral IFNT has been demonstrated insofar as the treatment of autoimmune diseases and cancer is concerned. The examples of the application that are relevant for these diseases (examples 5-11) use dosages of about 10^5 U/day. These examples are identically disclosed in 1, D2 and D4.

In conclusion, no technical effect has been demonstrated that was not already disclosed in the prior art and that could impart an inventive step to claims 1-6.

CLAIMS

1. Use of a composition comprising interferon-tau formulated for oral administration to the intestinal tract of the subject in an amount of ~~at least about 4.8×10^8~~ greater than about 1×10^9 Units/day for the preparation of a medicament for treating a condition in human subject responsive to interferon tau therapy, the condition selected from an autoimmune condition, or cancer, ~~or a viral infection other than hepatitis C~~, said amount being effective to produce an initial measurable increase in the subject's blood 2', 5'-oligoadenylate synthetase (OAS) level, relative to the blood OAS level in the subject in the absence of interferon-tau administration, wherein said interferon-tau is to be administered to the intestinal tract of the subject in such effective amount, on a regular basis of at least several times per week, for a period of at least one month, independent of changes in the subject's blood OAS level.

2. The use of claim 1, wherein said interferon-tau is an ovine interferon-tau having a sequence identified as SEQ ID NO:2 or SEQ ID NO:3.

3. The use of claim 1, wherein said interferon-tau is administered on a daily basis for a period of at least one month.

4. The use of claim 1, for treatment of multiple sclerosis in the subject, wherein said interferon-tau is to be administered during a period corresponding to presence of the subject's symptoms.

~~5. The use of claim 1, for treatment of a viral infection in the subject, wherein said interferon-tau is administered for a period of several months past the time when no viral infection is detected in the subject.~~

5. The use of claim 1, for treatment of cancer in the subject, wherein an anticancer agent is additionally to be administered to the subject during the period of interferon-tau administration.

6. The use of claim 1, wherein the subject's blood OAS level is monitored during administration of interferon-tau to ascertain if the OAS level is increased.

7.
8. A composition for use in preparation of a medicament for treating a condition in a human subject responsive to interferon-tau therapy, the condition selected from an autoimmune condition, or cancer, ~~or a viral infection other than hepatitis C~~, said composition comprising interferon-tau formulated for oral administration to the intestinal tract of the subject in an amount of ~~at least about 4.9×10^8~~ greater than about 1×10^8 Units/day, said amount being effective to produce an initial measurable increase in the subject's blood 2', 5'-oligoadenylate synthetase (OAS) level, relative to the blood OAS level in the subject in the absence of interferon-tau administration, wherein said interferon-tau is to be administered to the intestinal tract of the subject in such effective amount, on a regular basis of at least several times per week, for a period of at least one month, independent of changes in the subject's blood OAS level.